Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Belimumab (Benlysta®IV)	MP-RX-FP-11-23	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drugs

Service Description

This document addresses the use of *Belimumab (Benlysta®)* , a B-lymphocyte stimulator (BLyS)-specific inhibitor approved by the Food and Drug Administration (FDA) for the treatment of active, antibody-positive systemic lupus erythematosus (SLE) and active lupus nephritis, as add-on treatment to standard therapy, such as corticosteroids, antimalarials, and/or immunosuppressants.

Background Information

Benlysta is a human monoclonal antibody drug that specifically recognizes and inhibits the biological activity of B-lymphocyte stimulator, also known as B cell activation. Only the IV formulation of Benlysta was studied and approved in the pediatric population. Dosing between the IV and SC products differs in adult patients.

The American College of Rheumatology (ACR) uses the ACR classification criteria to diagnose an individual with SLE. The ACR requires 4 of these 11 criteria simultaneously or in succession for an individual to be classified as having SLE: malar rash, discoid rash, photosensitivity, oral ulcers, arthritis, serositis, renal disorders, neurological disorder, hematological disorder, immunological disorder, and anti-nuclear antibody.

The SELENA-SLEDAI (Safety of Estrogens in Systemic Lupus Erythematosus National Assessment -- Systemic Lupus Erythematosus Disease Activity Index) is a system used to evaluate the activity of lupus in clinical studies. This system is used for quantification of lupus disease, primarily for the purpose of determining whether a new drug evaluated for the disease is effective. The SELENA-SLEDAI is a slightly modified version of the SLEDAI and was developed by the NIH. It is a weighted index in which signs and symptoms, laboratory tests, and physician's assessment for each of nine organ systems are given a weighted score and summed up if present at the time of the visit or in the preceding 10 days. The maximum theoretical score for the SELENA-SEDAI is 105 (all 24 descriptors present simultaneously) with 0 indicating inactive disease.

Lupus nephritis (LN), or kidney inflammation, is one of the most common and serious complications of systemic lupus erythematosus (SLE), an autoimmune disease which causes widespread inflammation and tissue damage. If poorly controlled, LN may lead to irreversible kidney damage and the eventual need for dialysis or kidney transplant. BLISS (Belimumab in Subjects with SLE) study groups included adult patients with a diagnosis of SLE according the ACR, active disease with SELENA-SLEDAI score greater than or equal to 6, and anti-nuclear antibody (ANA) greater than or equal to 1:80 and/or anti-dsDNA greater than or equal to 30 IU/mL.

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BLISS (Belimumab in Subjects with SLE) study groups included adult patients with a diagnosis of SLE according the ACR, active disease with SELENA-SLEDAI score greater than or equal to 6, and anti-nuclear antibody (ANA) greater than or equal to 1:80 and/or anti-dsDNA greater than or equal to 30 IU/mL. Benlysta for SLE was also studied in pediatrics (5 to 17 years of age) in the PLUTO trial. Individuals had active disease with SELENA-SLEDAI score greater than or equal to 6, and positive ANA results. BLISS-LN study groups included adult patients with SLE and active lupus nephritis (class III, IV, or V) confirmed by renal biopsy. In both studies, Benlysta was added to standard therapy for treatment. Use of IV Benlysta for lupus nephritis in the pediatric population is based on extrapolation of efficacy from the adult study and supported by pharmacokinetic data. Safety and efficacy of subcutaneous Benlysta for lupus nephritis in the pediatric population has not been established. Additionally, of the subcutaneous devices for SLE, only the autoinjector has been studied in pediatrics, and not the prefilled syringe.

Approved Indications

A. Active, antibody-positive systemic lupus erythematosus (SLE) in patients 5 years of age and older who are receiving standard therapy.
B. Active lupus nephritis in patients 5 years of age and older who are receiving standard therapy.

Other Uses

i. N/A

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
J0490	Injection, belimumab, 10 mg [Benlysta]

ICD-10	Description
M32.10-M32.9	Systemic lupus erythematosus (SLE)

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Medical Necessity Guidelines

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met **all** approval criteria.*

Clinical Criteria

Belimumab (Benlysta®IV)

A. Criteria For Initial Approval

Initial requests for **intravenous** Benlysta (belimumab) may be approved if the following criteria are met:

i. Individual is 5 years of age or older and has a diagnosis of *Systemic Lupus Erythematosus* per the American College of Rheumatology (ACR); **AND**
   - A. Documentation is provided that disease is active and documented by a SELENA-SLEDAI score greater than or equal to 6 while on current treatment regimen for SLE; **AND**
   - B. Documentation is provided that individual has a positive anti-nuclear antibody (ANA) titer greater than or equal to 1:80 or anti-dsDNA greater than or equal to 30 IU/mL; **AND**
   - C. Individual's SLE disease remains active while on corticosteroids, antimalarials, or immunosuppressants (alone or as combination therapy) for at least the last 30 days; **AND**
   - D. Individual is using in combination with standard therapy (for example, corticosteroids, antimalarials, and/or immunosuppressants [but not other biologics]).

OR

ii. Individual is 5 years of age or older and has a diagnosis of *active Lupus Nephritis*; **AND**
   - A. Individual has Class III, IV, or V lupus nephritis showing active or chronic lesions, and confirmed by renal biopsy; **AND**
   - B. Documentation is provided that individual has a urinary protein to creatinine ratio of greater than or equal to 1; **AND**
   - C. Individual did not have disease progression to lupus nephritis while on Benlysta therapy for SLE without LN; **AND**
   - D. Individual's disease remains active while on corticosteroids, antimalarials, or immunosuppressants (alone or as combination therapy) for at least the last 30 days; **AND**
   - E. Individual is using in combination with standard therapy (for example, corticosteroids, antimalarials, and/or immunosuppressants [but not other biologics or IV cyclophosphamide]).

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B. Criteria For Continuation of Therapy

Continuation requests for Benlysta (belimumab IV) may be approved if the following criteria are met:

i. Documentation is provided for previous improvement in disease activity following treatment with Benlysta (belimumab) indicating a therapeutic response, including lack of disease progression to lupus nephritis while on Benlysta if initially only using for SLE without LN; **AND**
ii. Individual has no evidence of active central nervous system lupus (such as psychosis or seizures); **AND**
iii. Individual is using in combination with standard therapy (for example, corticosteroids, antimalarials, and/or immunosuppressants [but not other biologics or IV cyclophosphamide]).

C. Conditions not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

i. Individual has evidence of active central nervous system lupus (such as psychosis or seizures);

OR

ii. Individual is using in combination with IV cyclophosphamide (excluding cyclophosphamide use for **induction** therapy), voclosporin (Lupkynis), or intravenous immunoglobulin;

OR

iii. Individual is using in combination with another biologic, including rituximab or any other B cell targeted therapy, and anifrolumab-fnia (Saphnelo);

OR

iv. Individual has required treatment for an acute or chronic infection within the past 60 days (NCT00424476, NCT00410384);

OR

v. Individual has human immunodeficiency virus (HIV) infection, hepatitis B virus infection, or hepatitis C virus infection (NCT00424476, NCT00410384).

D. Authorization Duration

i. Approval Duration:
   a. Initial Approval Duration: 6 months
   b. Reauthorization Approval Duration: 1 year

Limits or Restrictions

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

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i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug	Recommended dosage and limit
Benlysta (belimumab) 120 mg, 400 mg vial for intravenous (IV) infusion	• Dosage: 10 mg/kg at 2-week intervals for the first 3 doses and at 4-week intervals thereafter • Limit: 10mg/kg every 4 weeks*
Exceptions	
*Initiation of therapy of Benlysta vials for IV infusion, may approve 10 mg/kg dosing at 2 week intervals for the first 3 doses.	

Reference Information

1. American College of Rheumatology (ACR). Guidelines for referral and management of systemic lupus erythematosus in adults. Arthritis & Rheumatism. 1999; 42(9): 1785-1796.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2022. URL: http://www.clinicalpharmacology.com. Updated periodically.
3. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: July 13, 2022.
4. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
5. Furie R, Petri M, Zamani O, et al. BLISS-76 Study Group. A phase III, randomized, placebo-controlled study of belimumab, a monoclonal antibody that inhibits B lymphocyte stimulator, in patients with systemic lupus erythematosus. Arthritis Rheum. 2011 Dec;63(12):3918-30. doi: 10.1002/art.30613.
6. Furie R, Rovin BH, Houssiau F, Malvar A, Teng YKO, Contreras G, Amoura Z, Yu X, Mok CC, Santiago MB, Saxena A, Green Y, Ji B, Kleoudis C, Burriss SW, Barnett C, Roth DA. Two-Year, Randomized, Controlled Trial of Belimumab in Lupus Nephritis. N Engl J Med. 2020 Sep 17;383(12):1117-1128. doi: 10.1056/NEJMoa2001180.
7. Furie R, Rovin BH, Houssiau F, Malvar A, Teng YKO, Contreras G, Amoura Z, Yu X, Mok CC, Santiago MB, Saxena A, Green Y, Ji B, Kleoudis C, Burriss SW, Barnett C, Roth DA. Two-Year, Randomized, Controlled Trial of Belimumab in Lupus Nephritis. N Engl J Med. 2020 Sep 17;383(12):1117-1128. doi: 10.1056/NEJMoa2001180.
8. Hahn BH, McMahon M, Wilkinson A, et. Al. American College of Rheumatology Guidelines for Screening, Case Definition, Treatment and Management of Lupus Nephritis. Arthritis Care Res (Hoboken). 2012 Jun; 64(6): 797-808. Doi: 10.1002/acr.21664. Available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3437757/.

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9. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2022; Updated periodically.
10. Navarra SV, Guzman RM, Gallacher AE, et al. BLISS-52 Study Group. Efficacy and safety of belimumab in patients with active systemic lupus erythematosus: a randomized, placebo-controlled, phase 3 trial. Lancet. 2011; 377(9767):721-731.
11. NCT00410384. U.S. National Library of Medicine, ClinicalTrials.gov website. https://clinicaltrials.gov/ct2/show/NCT00410384?term=nct+00410384&rank=1.
12. NCT00424476. U.S. National Library of Medicine, ClinicalTrials.gov website. https://clinicaltrials.gov/ct2/show/NCT00424476?term=nct+00424476&rank=1.
13. NCT01649765. U.S. National Library of Medicine, ClinicalTrials.gov website. https://clinicaltrials.gov/ct2/show/NCT01649765?term=nct+01649765&rank=1.
14. Centers for Medicare and Medicaid Services (CMS). Local Coverage Article (A52571): Self-Administered Drug Exclusion List. Retrieved from Article - Self-Administered Drug Exclusion List: (A52571) (cms.gov).

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

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Revision Type	Summary of Changes	P&T Approval Date	MPCC Approval Date
Annual Review 10/13/2025	Expansion to pediatric population in both SLE and LN. Remove restriction for use with cyclophosphamide. Coding reviewed: No changes.	10/31/2025	11/10/2025
Annual Review 11/26/2024	Update all sections to remove SC formulation from the medical policy (Part D drug). Update criteria for lupus nephritis to remove ANA/anti-dsDNA requirement. Clarify diagnosis requirements for SLE. Update recommended dosage table. Wording and formatting changes. Coding reviewed: No changes.	2/18/2025	3/6/2025
Policy Inception 11/20/2023	Elevance Health's Medical Policy adoption.	N/A	11/30/2023